

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
15 December 2005 (15.12.2005)

PCT

(10) International Publication Number
WO 2005/118548 A1

(51) International Patent Classification: C07D 217/18,
401/06, A61K 31/472, 31/4725, A61P 3/04, 25/00

(74) Agent: SCHAGER, Frank; Actelion Pharmaceuticals
Ltd, Gewerbestrasse 16, CH-4123 Allschwil (CH).

(21) International Application Number:
PCT/EP2005/001879

(22) International Filing Date: 23 February 2005 (23.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/EP2004/002020 1 March 2004 (01.03.2004) EP

(71) Applicant (for all designated States except US): ACTE-
LION PHARMACEUTICALS LTD [CH/CH]; Gewerbe-
strasse 16, CH-4123 Allschwil (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): WELLER, Thomas
[CH/CH]; Hoelzlistrasse 58, CH-4102 Binningen (CH).
KOBBERSTEIN, Ralf [DE/DE]; Boelenstrasse 17, 79539
Lürrach (DE). AISSAOUL, Hamed [FR/FR]; 4, allée de
Griottes, F-68840 Pulversheim (FR). CLOZEL, Martine
[FR/CH]; Winterhalde 3b, CH-4102 Binningen (CH).
FISCHLI, Walter [CH/CH]; Obertorweg 64, CH-4123
Allschwil (CH).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW.

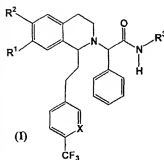
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED 1,2,3,4-TETRAHYDROISOQUINOLINE DERIVATIVES



(57) Abstract: The invention relates to novel 1,2,3,4-tetrahydroisoquinoline derivatives of formula (I) wherein R¹, R², R³ and X are as defined in the claims, and their use as active ingredients in the preparation of pharmaceutical compositions. The invention also concerns related aspects including processes for the preparation of the compounds, pharmaceutical compositions containing one or more of those compounds and methods of treatment comprising administration of said compounds to a mammal.